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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/808,205 | 03/24/2004 | Suzanne T. ILdstad | 17541-040001 | 3925 |

26191 7590 06/07/2007
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| EXAMINER | |
|---|---|
| SKELDING, ZACHARY S | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1644 | |

| MAIL DATE | DELIVERY MODE |
|---|---|
| 06/07/2007 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/808,205 | IIDSTAD, SUZANNE T. | |
| | Examiner | Art Unit | |
| | Zachary Skelding | 1644 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *08 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) *1-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10-29-04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

1. Applicant's election of Group XVI, in the response filed March 8, 2007 is acknowledged.

   Claims 1-30 are pending.

2. Applicant election of the invention of Group XVI and the species "diabetes," with traverse, is acknowledged. However, because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

   Thus, the Restriction Requirement of January 16, 2007 is made **FINAL**.

   Nevertheless, upon further consideration, the election of species requirement, as it applies to Group XVI, has been withdrawn.

   **Accordingly, claims 28-30 are under examination** as they read on a method for conditioning a recipient for bone marrow transplantation comprising subjecting the recipient to total body irradiation and infusing the recipient with a donor cell preparation containing hematopoietic stem cells various days after total body irradiation.

   **Furthermore, claims 1-27 have been withdrawn** from further consideration by the Examiner, under 37 C.F.R. § 1.142(b), as being directed to a non-elected invention.

3. The application is required to be reviewed and all spelling, TRADEMARKS, and like errors corrected.

   The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which Applicant may become aware in the specification.

   Applicant's IDS, filed October 29, 2004, has been considered.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

   > The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 28-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

**A. Preamble vs. Steps**

Claims 28-30 are drawn to "a method for conditioning a recipient ***for bone marrow transplantation*** comprising subjecting said recipient to a total dose of total body irradiation...and ***infusing the recipient with a donor cell preparation containing hematopoietic stem cells***..."

The phrase, "infusing the recipient with a donor cell preparation containing hematopoietic stem cells," given its broadest reasonable interpretation consistent with the instant specification and with the knowledge of the skilled artisan as of applicant's filing date, is being read as a preparation of cells comprising hematopoietic stem cells, i.e., cells capable of engrafting into the recipient's bone marrow and producing blood cells.

***However, claims 28-30 are indefinite in that*** the preamble of claims 28-30 recites "a method for ***conditioning a recipient*** <u>for</u> ***bone marrow transplantation***," while the steps recite "infusing the recipient with a donor cell preparation containing hematopoietic stem cells from the donor..." and thus it is unclear if the step of "infusing the recipient with a donor cell preparation containing hematopoietic stem cells from the donor..." includes infusion with bone marrow as bone marrow contains hematopoietic stem cells or if this is excluded by the preamble.

**B. Further uncertainty about whether the preamble is limiting or not**

Further uncertainty about the meaning of the preamble recited in the instant claims comes from applicant's assertion in their Remarks of March 8, 2007, that the instant claims are "...***<u>not</u> directed toward methods for partially or completely reconstituting a mammal's lymphohematopoietic system".***

However, in contrast to applicant's assertions, claims drawn to a method comprising infusing a recipient who has been subjected to total body irradiation with "a donor cell preparation comprising hematopoietic stem cells" would appear to read on "a method for partially or completely reconstituting a mammal's lymphohematopoietic system" since ***this is what hematopoietic stem cells will do when infused into a recipient who has been previously treated with total body irradiation, i.e., hematopoietic stem cells will home to the bone marrow and give rise to new blood cells.***

Thus, in light of the apparent contradiction between the claim preamble/applicant's assertions in their Remarks of March 8, 2007 versus the claim steps, the skilled artisan would not be reasonably appraised of the metes and bounds of the invention.

It should be further noted that withdrawn claims 16 and 25 serve to further illustrate the indefiniteness of the instant claims.

More particularly, as essentially stated in the Restriction Requirement of January 16, 2007, like claims 28-30, the preamble of withdrawn claim 25 recites "a method for conditioning a recipient for bone marrow transplantation comprising..." and the steps recited in claim 25 recite irradiation and "administering hematopoietic stem cells from a donor." Thus, like claims 28-30, claim 25 is directed to both irradiating a recipient and infusing hematopoietic stem cells into the recipient.

In contrast, withdrawn claim 16, which is substantially identical to claim 25, recites in its preamble "a method for partially or completely reconstituting a mammal's lymphohematopoietic system comprising...".

Thus, withdrawn claims 16 and 25 serve to further illustrate the uncertainty associated with how claims with the preamble "a method for conditioning a recipient for bone marrow transplantation comprising...," such as claims 25 and 28-30, are to be interpreted in light of claims which recite nearly the same steps, such as claim 16, but have a ***substantially different preamble***, "a method for partially or completely reconstituting a mammal's lymphohematopoietic system comprising...".

Applicant is reminded that any amendment to the claims must point to a basis in the specification so as not to add any new matter. See MPEP 714.02 and 2163.06.

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 28-30 are rejected under 35 U.S.C. § 102(b) as anticipated by Sykes et al. (WO 02/40049)(see entire document).

As a preliminary matter, it should be noted that the instant claims recite "...infusing the recipient with a donor cell preparation ***containing*** hematopoietic stem cells...," where the phrase "***containing*** hematopoietic stem cells" given its broadest reasonable interpretation consistent with the instant specification, is being read as "***comprising*** hematopoietic stem cells," since, as stated in MPEP § 2111.03, "the transitional term 'comprising'...is synonymous with ...'containing'..."

Sykes teaches that conditioning of the recipient for allogenic bone marrow transplantation activates pro-inflammatory cytokines which promotes graft-versus-host- disease (see, in particular, page 8, 1st paragraph). However, Sykes further teaches that graft-versus-host-disease can be decreased by the use of less pro-inflammatory conditioning regimes, for example low dose total body irradiation, followed by delayed administration of a donor cell preparation containing hematopoietic stem cells (see, in particular, page 8, 1st paragraph; page 16, 2nd to page 18, 1st paragraph, in particular page 17, 1st paragraph). For example, Sykes teaches a method comprising administering to a recipient a total dose of total body irradiation of, for example, less than 200 cGy, followed by infusion, 1, 2, 3, 4 or 5 days after total body irradiation, with a donor cell preparation containing hematopoietic stem cells (see, in particular, page 16, 2nd paragraph and page 12, 2nd-4th paragraphs, noting that "rad" and "cgy" are equivalent units).

Thus, Sykes anticipates the instant claims.

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claim 28 is rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-18 of U.S. Patent No. 5,514,364 (cited herewith); claim 2 of U.S. Patent No. 5,635,156 (cited on applicant's IDS of October 29, 2004), and claim 2 of U.S. Patent No. 5,876,692 (cited on applicant's IDS of October 29, 2004). Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claim is anticipated by the claims of the reference claims.

In particular, the reference claims are drawn to a method for conditioning a recipient for bone marrow transplantation comprising administering between 1 and 7 Gy total body irradiation, followed by transplantation with a donor cell preparation containing hematopoietic stem cells.

For the purposes of double patenting examination, the reference claims are being examined as they read on infusion of the hematopoietic stem cells into the recipient ***immediately after*** total body irradiation.

Thus, the instant claim is unpatentable over the reference claims.

10. Claims 28 and 29 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 2 of U.S. Patent No. 5,635,156 and claim 2 of U.S. Patent No. 5,876,692, each in view of Sykes et al. (WO 02/40049).

More particularly, the reference claims are drawn to methods for conditioning a recipient for bone marrow transplantation comprising administering between 1 Gy and 5 Gy of total body irradiation, followed by transplantation with a donor cell preparation containing hematopoietic stem cells.

For the purposes of double patenting examination, the reference claims are being examined as they read on infusion of the hematopoietic stem cells into the recipient ***immediately after*** total body irradiation.

The instant claims differ from the claims of the reference teachings in that infusion of the hematopoietic stem cells into the recipient occurs at least 1 day after total body irradiation.

Sykes teaches that conditioning of the recipient for allogenic bone marrow transplantation activates pro-inflammatory cytokines which promote graft-versus-host-disease (see, in particular, page 8, 1st paragraph). Moreover, Sykes further teaches that graft-versus-host-disease can be decreased by the use of less pro-inflammatory conditioning regimes, for example low dose total body irradiation, followed by delayed administration of a donor cell preparation containing hematopoietic stem cells (see, in particular, page 8, 1st paragraph; page 16, 2nd to page 18, 1st paragraph, in particular page 17, 1st paragraph). For example, Sykes teaches a method comprising administering to a recipient a total dose of total body irradiation of, for example, less than 200 cGy, followed by infusion, 1, 2, 3, 4 or 5 days after total body irradiation, with a donor cell preparation containing hematopoietic stem cells (see, in particular, page 16, 2nd paragraph and page 12, 2nd-4th paragraphs, noting that "rad" and "cgy" are equivalent units).

One of ordinary skill in the art would have been motivated to apply the teachings of Sykes to delay transplantation of the donor cell preparation containing hematopoietic stem cells until 1, 2, 3, 4 or 5 days after total body irradiation to the reference claims in order to minimize graft-versus-host-disease. As is well known to one of ordinary skill in the art, minimizing graft-versus-host-disease is useful because this is a dangerous side effect associated with transplantation of donor cell preparations containing hematopoietic stem cells and because by generally decreasing graft versus host disease one can potentially perform more transplants of allogenic donor cell preparation containing hematopoietic stem cells which are far more available than autologous cell preparation containing hematopoietic stem cells.

Thus, the instant claims are unpatentable over the reference claims in view of Sykes.

11. Claim 28 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over copending:

Claims 18-20 of USSN 10/702,058;
Claims 11-13, 23 and 26 of USSN 10/134,016;
Claims 7, 11-13 of USSN 10/558,513; and
Claim 2 of USSN 10/558,516

Although the conflicting claims are not identical, they are not patentably distinct from each other because the reference claims are drawn to a method for conditioning a recipient for bone marrow transplantation comprising administering between 1 and 7 Gy total body irradiation, followed by transplantation with a donor cell preparation containing hematopoietic stem cells.

For the purposes of double patenting examination, the reference claims are being examined as they read on infusion of the hematopoietic stem cells into the recipient ***immediately after*** total body irradiation.

Thus, the instant claim is unpatentable over the reference claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

12. Claims 28 and 29 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable as being unpatentable over copending:

Claims 18-20 of USSN 10/702,058;
Claims 11-13, 23 and 26 of USSN 10/134,016;
Claims 7, 11-13 of USSN 10/558,513; and
Claim 2 of USSN 10/558,516,

each in view of Sykes et al. (WO 02/40049).

More particularly, the reference claims are drawn to methods for conditioning a recipient for bone marrow transplantation comprising administering between 1 Gy and 5 Gy of total body irradiation, followed by transplantation with a donor cell preparation containing hematopoietic stem cells.

For the purposes of double patenting examination, the reference claims are being examined as they read on infusion of the hematopoietic stem cells into the recipient ***immediately after*** total body irradiation.

The instant claims differ from the claims of the reference teachings in that infusion of the hematopoietic stem cells into the recipient occurs at least 1 day after total body irradiation.

Sykes teaches that conditioning of the recipient for allogenic bone marrow transplantation activates pro-inflammatory cytokines which promote graft-versus-host-disease (see, in particular, page 8, 1st paragraph). Moreover, Sykes further teaches that graft-versus-host-disease can be decreased by the use of less pro-inflammatory conditioning regimes, for example low dose total body irradiation, followed by delayed administration of a donor cell preparation containing hematopoietic stem cells (see, in particular, page 8, 1st paragraph; page 16, 2nd to page 18, 1st paragraph, in particular page 17, 1st paragraph). For example, Sykes teaches a method comprising administering to a recipient a total dose of total body irradiation of, for example, less than 200 cGy, followed by infusion, 1, 2, 3, 4 or 5 days after total body irradiation, with a donor cell preparation containing hematopoietic stem cells (see, in particular, page 16, 2nd paragraph and page 12, 2nd-4th paragraphs, noting that "rad" and "cgy" are equivalent units).

One of ordinary skill in the art would have been motivated to apply the teachings of Sykes to delay transplantation of the donor cell preparation containing hematopoietic stem cells until 1, 2, 3, 4 or 5 days after total body irradiation to the reference claims in order to minimize graft-versus-host-disease. As is well known to one of ordinary skill in the art, minimizing graft-versus-host-disease is useful because this is a dangerous side effect associated with transplantation of donor cell preparations containing hematopoietic stem cells and because by generally decreasing graft versus host disease one can potentially perform more transplants of allogenic donor cell preparation containing hematopoietic stem cells which are far more available than autologous cell preparation containing hematopoietic stem cells.

Thus, the instant claims are unpatentable over the reference claims in view of Sykes.

This is a provisional obviousness-type double patenting rejection.

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachary Skelding whose telephone number is 571-272-9033. The examiner can normally be reached on Monday - Friday 8:00 a.m. - 5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Zachary Skelding, Ph.D.
Patent Examiner
May 16, 2007

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TC 1600
5/19/07